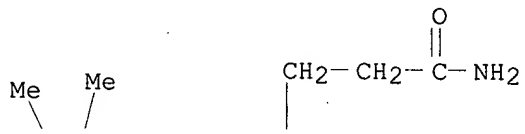
L5 ANSWER 1 OF 7 REGISTRY COPYRIGHT 2001 ACS
RN 247215-83-4 REGISTRY
CN Cobinamide, Ne,Ne'-[[5-[[4-(tributylstannyl)benzoyl]amino]-1,3-phenylene]bis(15-oxo-4,7,10-trioxa-14-azapentadecane-15,1-diyl)]bis[Co-(cyano-.kappa.C)-, bis(dihydrogen phosphate) (ester), bis(inner salt), P.fwdarw.3':P'.fwdarw.3'''diester with (5,6-dimethyl-1-.alpha.-D-ribofuranosyl-1H-benzimidazole-.kappa.N3) (9CI) (CA INDEX NAME)
MF C173 H251 Co2 N31 O37 P2 Sn
CI CCS
SR CA
LC STN Files: CA, CAPLUS

PAGE 1-A



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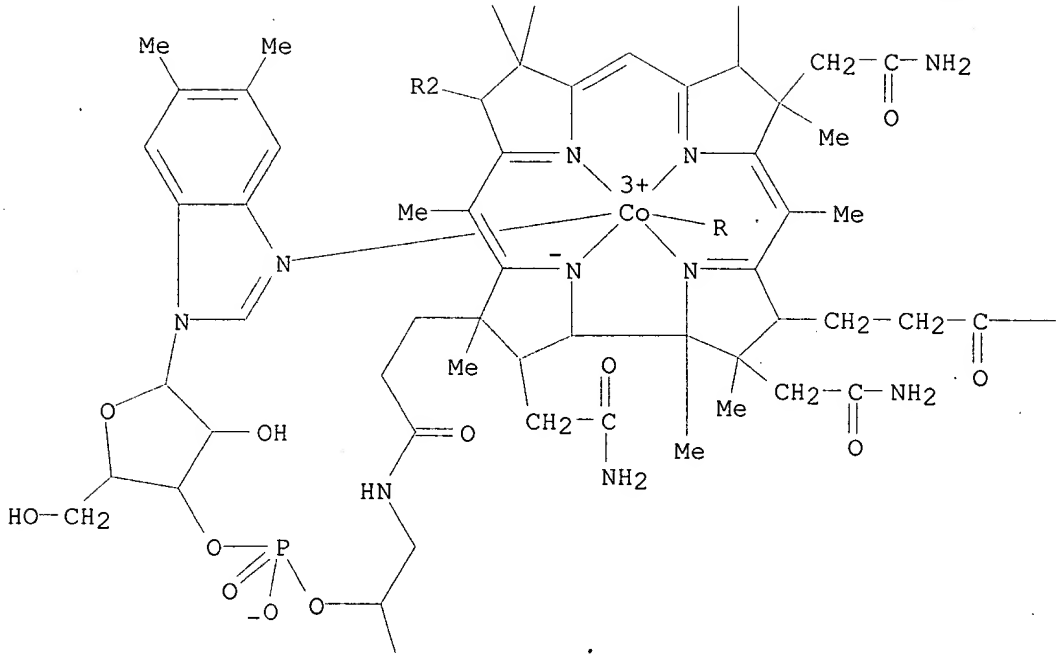
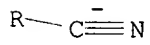
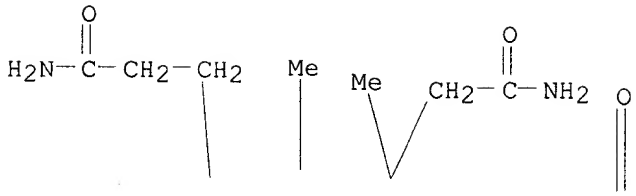


PAGE 2-B

— NH_2


Me


R
C
N


O
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C
CH2
CH2
Me
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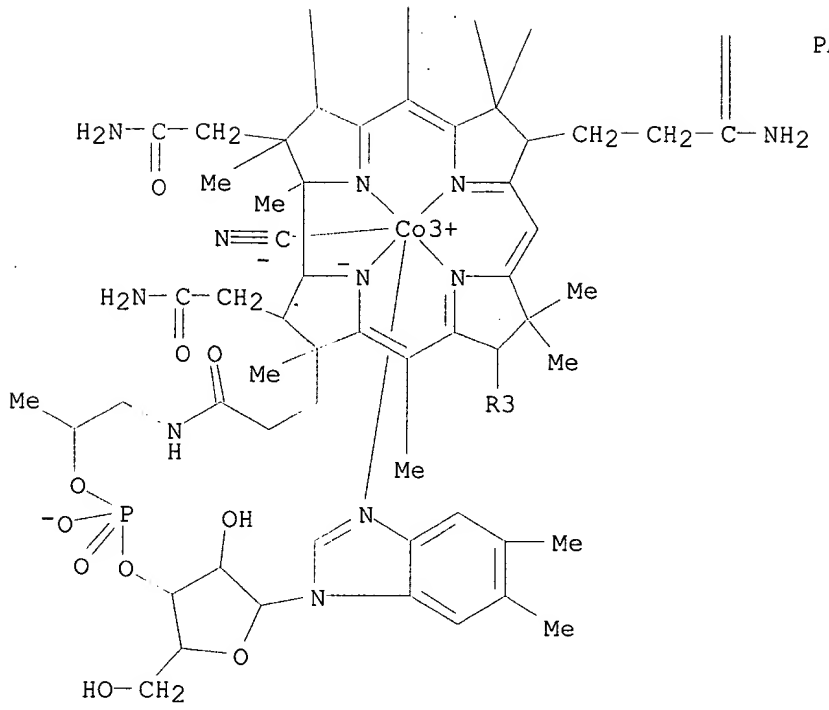
CH2
C
NH2
O

PAGE 4-A



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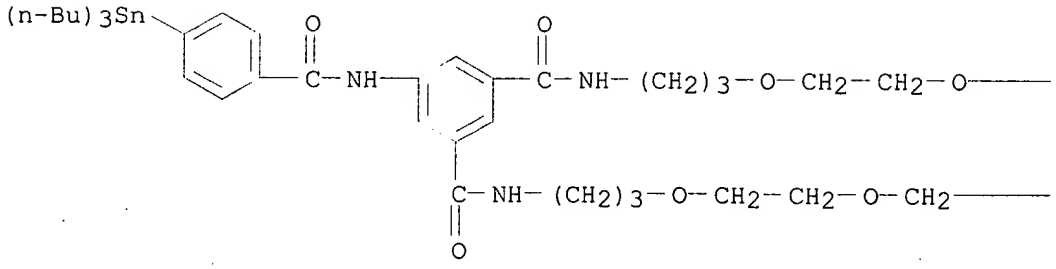
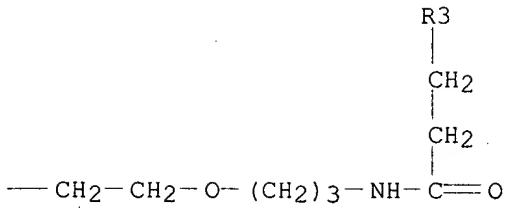
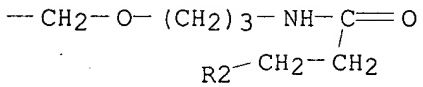






1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:308530 Radioiodination of Cyanocobalamin Conjugates Containing Hydrophilic Linkers: Preparation of a Radioiodinated Cyanocobalamin Monomer and Two Dimers, and Assessment of Their Binding with Transcobalamin II. Wilbur, D. Scott; Pathare, Pradip M.; Hamlin, Donald K.; Rothenberg, Sheldon P.; Quadros, Edward V. (Department of Radiation Oncology, University of Washington, Seattle, WA, 98195, USA). Bioconjugate Chem., 10(5), 912-920 (English) 1999. CODEN: BCCHES. ISSN: 1043-1802. Publisher: American Chemical Society.

AB This report describes an investigation aimed at prepn. of radioiodinated cyanocobalamin (CN-Cbl) monomers and dimers with improved water soly. and decreased nonspecific binding. In the investigation, synthesis and radioiodination reactions of one monomeric and two dimeric CN-Cbl derivs. were conducted. The initial step in the synthesis of the CN-Cbl derivs. was mild acid hydrolysis of CN-Cbl, 1, followed by sepn. of the resultant corrin ring b-, d-, and e-monocarboxylate isomers. The investigation was limited to prepn. of conjugates of CN-Cbl-e-carboxylate, 2, as earlier studies had shown binding of that isomer with recombinant human transcobalamin II (rhTCII) was similar to CN-Cbl. In a second synthetic step, the hydrophilic linker moiety, 4,7,10-trioxa-1,13-tridecandiamine, 3, was conjugated with 2 to form the adduct, 4. The synthesis of a monomeric CN-Cbl deriv., 6a, which can be used for radioiodination, was accomplished by reaction of 4 with p-tri-n-butylstannylbenzoate tetrafluorophenyl (TFP) ester, 5a. Two CN-Cbl dimers contg. the arylstannane radioiodination moiety were also synthesized. The first dimer, 8a, was synthesized by crosslinking 4 with a stannylbenzoyl-aminoisophthalate di-TFP ester, 7a. The second dimer, 11a, was synthesized by reacting benzene tricarboxylate tri-TFP ester, 10, in a stepwise manner with 1 equiv of the adduct of 5a and 3 (forming 9a), followed by 2 equiv of 4. Iodobenzoate HPLC stds., 6b, 8b, and 11b, used in the radioiodination studies, were prepd. in a manner similar to that of the stannylbenzoate derivs. Radioiodinations were performed by reacting 6a, 8a, or 11a with N-chlorosuccinimide and Na[125I]I in methanol under neutral conditions. Radiochem. yields of 17-42% were obtained. Evaluation of the binding properties of radiolabeled CN-Cbl conjugates

with rhTCII showed that the dimer of CN-Cbl, 11b, bound more avidly than the monomer, 6b, and that the binding affinity of the dimer is essentially equiv. to that of unmodified CN-Cbl. Incubation of radioiodinated monomer, [125I]6b, and dimer, [125I]11b, with rhTCII followed by size-exclusion chromatog. anal. provided data that the monomer bound one rhTCII mol. whereas two rhTCII mols. were bound to approx. 30% of the dimer.

L5 ANSWER 2 OF 7 REGISTRY COPYRIGHT 2001 ACS
RN 199672-74-7 REGISTRY
CN 1,3-Benzenedicarboxylic acid, dihydrazide, polymer with bis(isocyanatomethyl)benzene, L 1050 and tin chloride (SnCl2) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Benzene, bis(isocyanatomethyl)-, polymer with 1,3-benzenedicarboxylic acid dihydrazide, L 1050 and tin chloride (SnCl2) (9CI)
CN L 1050, polymer with 1,3-benzenedicarboxylic acid dihydrazide, bis(isocyanatomethyl)benzene and tin chloride (SnCl2) (9CI)
CN Tin chloride (SnCl2), polymer with 1,3-benzenedicarboxylic acid dihydrazide, bis(isocyanatomethyl)benzene and L 1050 (9CI)
MF (C10 H8 N2 O2 . C8 H10 N4 O2 . Cl2 Sn . Unspecified)x
CI PMS
PCT Manual component, Polyother, Polyother only
SR CA
LC STN Files: CA, CAPLUS

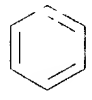
CM 1

CRN 199618-53-6
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

CRN 25854-16-4
CMF C10 H8 N2 O2
CCI IDS



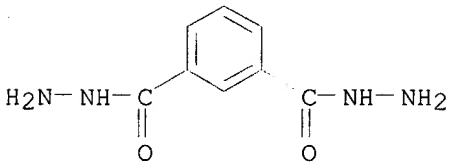
2 [D1—CH_2—NCO]

CM 3

CRN 7772-99-8
CMF Cl2 Sn

CM 4

CRN 2760-98-7
CMF C8 H10 N4 O2



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 128:102699 Electric properties of linear polyurethanes. Savel'ev, Yu. v; Grekov, A. P.; Kuporev, B. A.; Kuznetsov, S. V.; Ogorodova, T. N. (Inst. Khim. Vysokomol. Soedin., NAN Ukr., Kiev, Ukraine). Ukr. Khim. Zh. (Russ. Ed.), 63(3-4), 60-65 (Russian) 1997. CODEN: UKZHAU. ISSN: 0041-6045. Publisher: Institut Obshchei i Neorganicheskoi Khimii NAN Ukrainy.

AB The elec. properties of the polyurethanes and the effect of metal complexes and metal salts, incorporated both in the basic macro chain of the polyurethanes and in the polymer matrix as modifying agents were investigated. The influence of the polymer's ability to the complexation with macrochain's fragments and magnetic descriptions of the central metal atoms on the elec. properties of the polymers were shown.

L5 ANSWER 3 OF 7 REGISTRY COPYRIGHT 2001 ACS
RN 199533-75-0 REGISTRY
CN 1,3-Benzenedicarboxylic acid, dihydrazide, polymer with bis(isocyanatomethyl)benzene, p 1000 (Dai-ichi polyol) and tin chloride (SnCl2) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Benzene, bis(isocyanatomethyl)-, polymer with 1,3-benzenedicarboxylic acid dihydrazide, p 1000 (Dai-ichi polyol) and tin chloride (SnCl2) (9CI)
CN P 1000 (Dai-ichi polyol), polymer with 1,3-benzenedicarboxylic acid dihydrazide, bis(isocyanatomethyl)benzene and tin chloride (SnCl2) (9CI)
CN Tin chloride (SnCl2), polymer with 1,3-benzenedicarboxylic acid dihydrazide, bis(isocyanatomethyl)benzene and p 1000 (Dai-ichi polyol) (9CI)
MF (C10 H8 N2 O2 . C8 H10 N4 O2 . Cl2 Sn . Unspecified)x
CI PMS

PCT Manual component, Polyother, Polyurethane, Polyurethane formed
SR CA
LC STN Files: CA, CAPLUS

CM 1

CRN 53528-83-9
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

CRN 25854-16-4
CMF C10 H8 N2 O2
CCI IDS

2 [D1—CH_2—NCO]

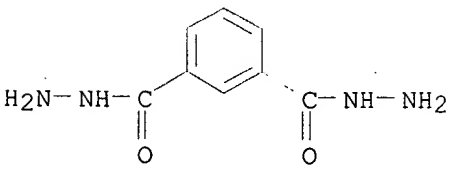
CM 3

CRN 7772-99-8
CMF Cl2 Sn

Cl—Sn—Cl

CM 4

CRN 2760-98-7
CMF C8 H10 N4 O2



1 REFERENCES IN FILE CA (1967 TO DATE)
Prepared by M. Hale 308-4258

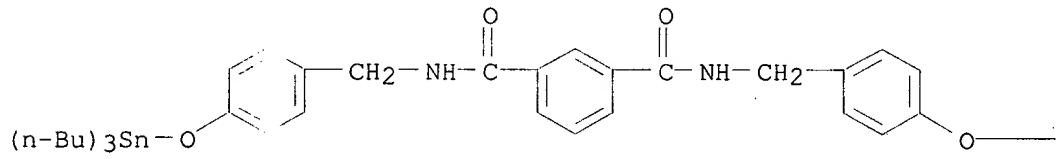
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 128:102699 Electric properties of linear polyurethanes. Savel'ev, Yu. v; Grekov, A. P.; Kuporev, B. A.; Kuznetsov, S. V.; Ogorodova, T. N. (Inst. Khim. Vysokomol. Soedin., NAN Ukr., Kiev, Ukraine). Ukr. Khim. Zh. (Russ. Ed.), 63(3-4), 60-65 (Russian) 1997. CODEN: UKZHAU. ISSN: 0041-6045. Publisher: Institut Obshchei i Neorganicheskoi Khimii NAN Ukrainy.

AB The elec. properties of the polyurethanes and the effect of metal complexes and metal salts, incorporated both in the basic macro chain of the polyurethanes and in the polymer matrix as modifying agents were investigated. The influence of the polymer's ability to the complexation with macrochain's fragments and magnetic descriptions of the central metal atoms on the elec. properties of the polymers were shown.

L5 ANSWER 4 OF 7 REGISTRY COPYRIGHT 2001 ACS
RN 175689-90-4 REGISTRY
CN 1,3-Benzenedicarboxamide, N,N'-bis[[4-[(tributylstannyl)oxy]phenyl]methyl]- (9CI) (CA INDEX NAME)
MF C46 H72 N2 O4 Sn2
SR CA
LC STN Files: CA, CAPLUS

PAGE 1-A



PAGE 1-B

Sn(Bu-n)3

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 124:289497 Catenane chameleons: environment-sensitive translational isomerism in amphiphilic benzylic amide [2]catenanes. Leigh, David A.; Moody, Karen; Smart, John P.; Watson, Karen J.; Slawin, Alexandra M. Z. (Dep. Chemistry, Univ. Manchester Institute Science Technology, Manchester, M60 1QD, UK). Angew. Chem., Int. Ed. Engl., 35(3), 306-10 (English) 1996. CODEN: ACIEAY. ISSN: 0570-0833.

AB The synthesis, structure and properties of a new class of constitutionally

simple, but topol. complex, compds. contg. amphiphilic units connected by noncovalent, mech. linkages to form catenanes are reported. The amphiphilic benzylic amide catenanes described illustrate how the noncovalent assembly of even the simplest of mols. can result in materials with remarkable and unexpected properties by virtue of their supramol. architectures.

L5 ANSWER 5 OF 7 REGISTRY COPYRIGHT 2001 ACS
RN 173341-54-3 REGISTRY
CN Cobinamide, Nd,Nd'-[[5-[[4-(tributylstannyl)benzoyl]amino]-1,3-phenylene]bis(carbonylimino-12,1-dodecanediyl)]bis[Co-(cyano-.kappa.C)-, bis(dihydrogen phosphate) (ester), bis(inner salt), 3',3''-diester with (5,6-dimethyl-1-.alpha.-D-ribofuranosyl-1H-benzimidazole-.kappa.N3) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Cobinamide, Nd,Nd'-[[5-[[4-(tributylstannyl)benzoyl]amino]-1,3-phenylene]bis(carbonylimino-12,1-dodecanediyl)]bis-, dicyanide, bis(dihydrogen phosphate) (ester), bis(inner salt), 3',3''-diester with 5,6-dimethyl-1-.alpha.-D-ribofuranosyl-1H-benzimidazole
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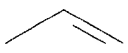
CI CCS
SR CA
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL



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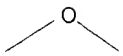

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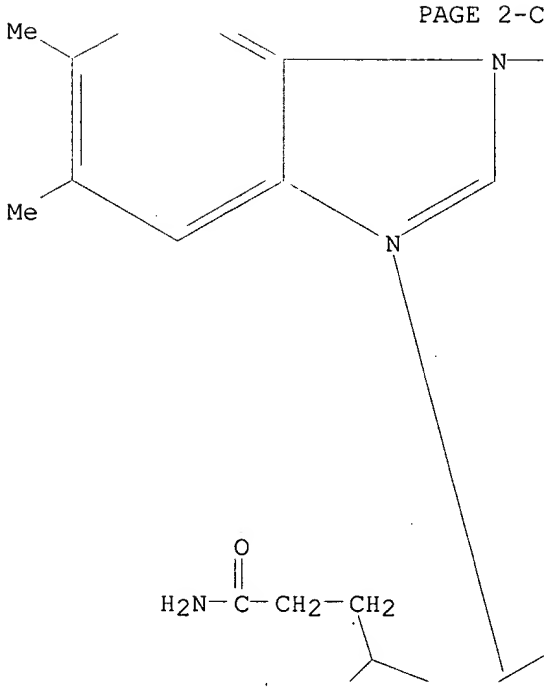

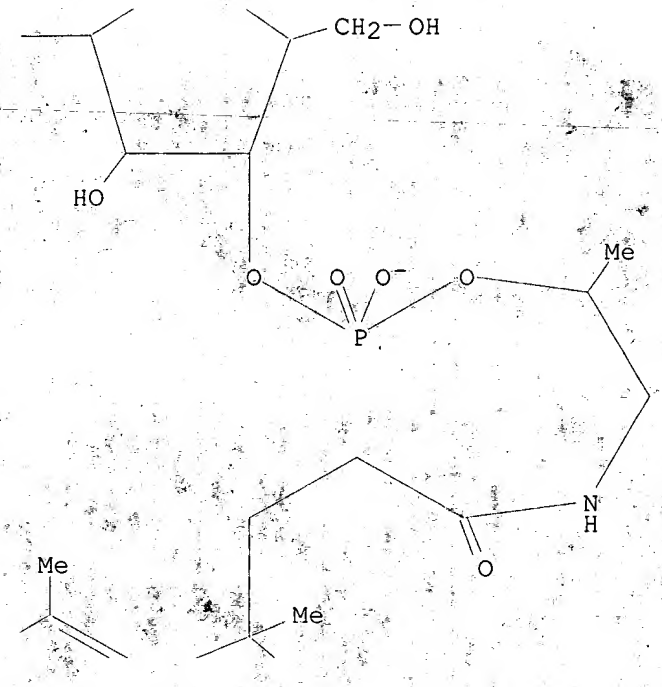
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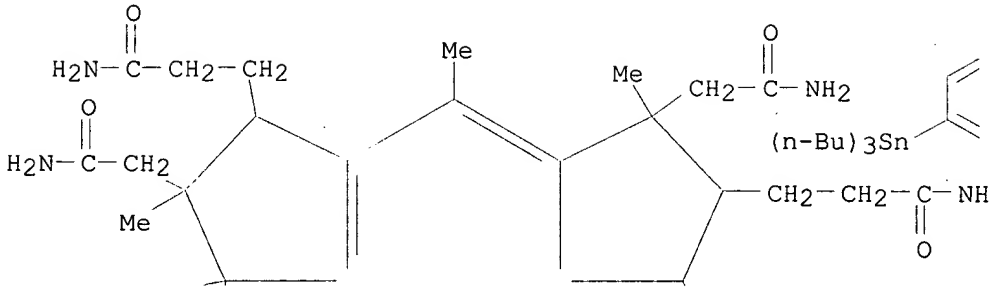
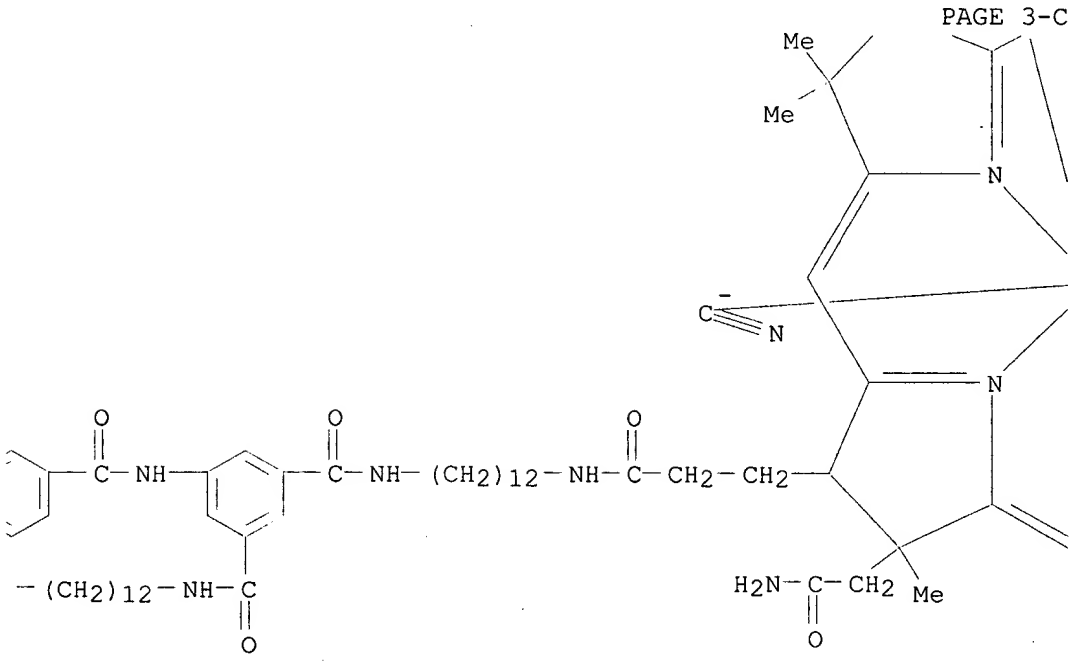
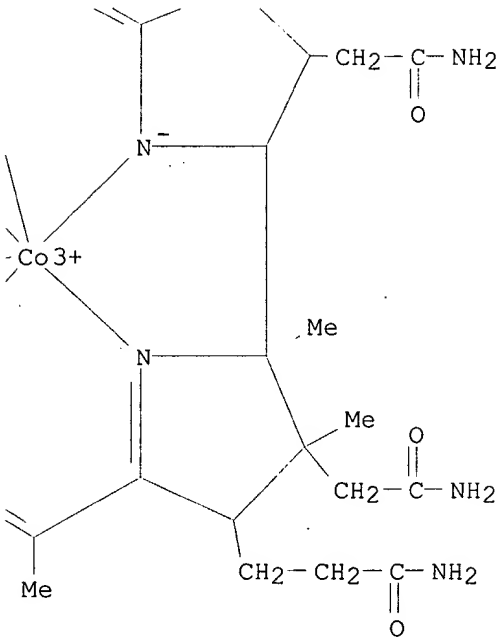
O
O⁻
P
O
Me
N
H
O
Me
Me



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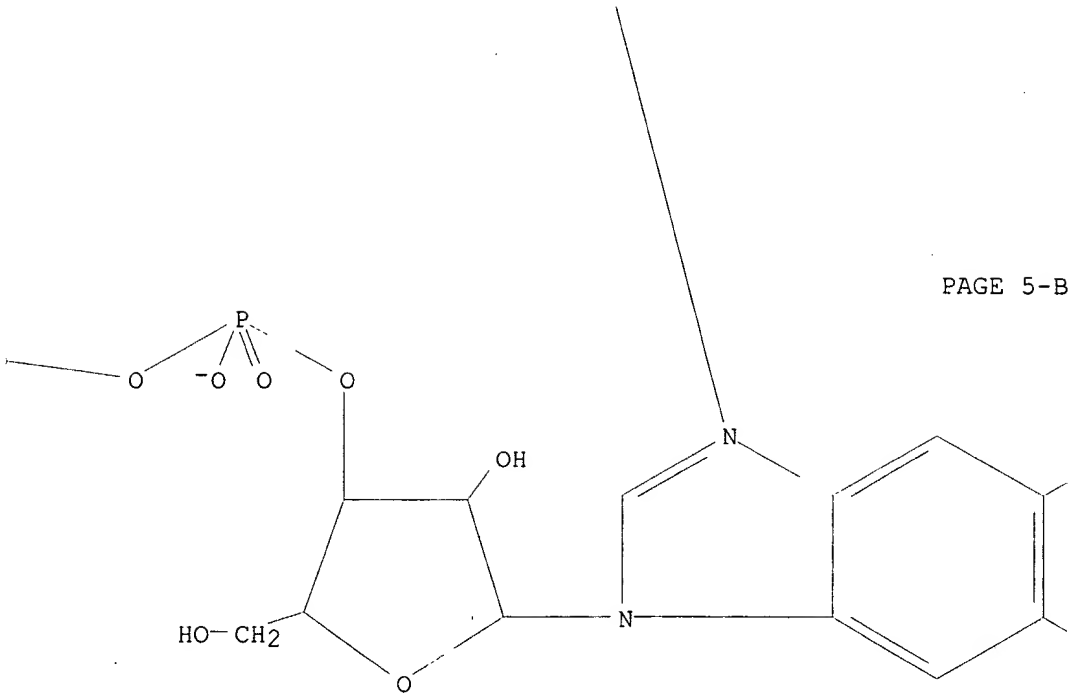
O
N
Co3+
N
Me
Me
O
CH2—C—NH2
Me
CH2—CH2—C—NH2
O

PAGE 4-A

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 5-A

PAGE 5-B



PAGE 5-C

Me

Me

7 REFERENCES IN FILE CA (1967 TO DATE)
7 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:177546 Methods of receptor modulation and therapeutic and diagnostic uses therefor. Morgan, A. Charles, Jr.; Wilbur, D. Scott (Receptagen Corporation, USA; University of Washington). U.S. US 5869465 A 19990209, 47 pp., Cont.-in-part of U.S. Ser. No. 224,831, abandoned. (English). CODEN: USXXAM. APPLICATION: US 1995-406194 19950316. PRIORITY: US 1994-224831 19940408.

AB Receptor-modulating agents capable of modulating cell surface receptors by

affecting the cell-surface receptor trafficking pathway are utilized for the treatment and diagnosis of a variety of disorders in warm-blooded animals, including neoplastic disorders. The receptor-modulating agents are comprised of a covalently bound rerouting moiety and targeting moiety.

Synthesis of several receptor-modulating agents using different functional classes of rerouting moieties is described. More specifically, a series of examples are presented which employ vitamin B12 as a targeting moiety in a receptor-modulating agent.

REFERENCE 2: 130:38642 Preparation of water soluble vitamin B12 as antiinflammatory receptor modulating agents. Morgan, A. Charles, Jr.; Wilbur, D. Scott (Receptagen Corporation, USA; University of Washington). U.S. US 5840880 A 19981124, 50 pp., Cont.-in-part of U.S. Ser. No. 224,831, abandoned. (English). CODEN: USXXAM. APPLICATION: US 1995-406191 19950316. PRIORITY: US 1994-224831 19940408.

AB Vitamin B12 antiinflammatory receptor modulating agents capable of modulating cell surface receptors by affecting the cell surface receptor trafficking pathway are disclosed. The vitamin B12 receptor modulating agents are comprised of a covalently bound rerouting moiety and targeting moiety linked by a water-solubilizing linker. Synthesis of a vitamin B12/biotin conjugate and fusion protein receptor modulating agent is reported.

REFERENCE 3: 130:38641 Preparation of water soluble vitamin B12 as antiinflammatory receptor modulating agents. Morgan, A. Charles, Jr.; Wilbur, D. Scott; Pathare, Pradip M. (Receptagen Corporation, USA; University of Washington). U.S. US 5840712 A 19981124, 66 pp., Cont.-in-part of U.S. Ser. No. 406,191. (English). CODEN: USXXAM. APPLICATION: US 1995-545151 19951019. PRIORITY: US 1994-224831 19940408; US 1995-406191 19950316; US 1995-406192 19950316; US 1995-406194 19950316.

AB Vitamin B12 antiinflammatory receptor modulating agents capable of modulating cell surface receptors by affecting the cell surface receptor trafficking pathway are disclosed. The vitamin B12 receptor modulating agents are comprised of a covalently bound rerouting moiety and targeting moiety linked by a water-solubilizing linker. Synthesis of a vitamin B12/biotin conjugate and fusion protein receptor modulating agent is reported.

REFERENCE 4: 128:295003 Preparation of biotinylated cobalamins as antiinflammatory agents and transcobalamin II receptors. Wilbur, D. Scott; Pathare, Pradip M.; Morgan, A. Charles, Jr. (University of Washington, USA; Receptagen Corp.). U.S. US 5739287 A 19980414, 58 pp. Cont.-in-part of U.S. Ser. No. 224,831, abandoned. (English). CODEN: USXXAM. APPLICATION: US 1995-406192 19950316. PRIORITY: US 1994-224831 19940408.

AB A biotinylated cobalamin, formed from a vitamin B12 mol. coupled to a biotin mol., is disclosed. In a preferred embodiment, the vitamin B12 mol. is cyanocobalamin. The biotin mol. can also be coupled to a rerouting moiety, optionally through a biotin binding protein such as avidin or streptavidin. The biotinylated cobalamin binds to a cell surface receptor, is invaginated, and once internalized affects the receptor trafficking pathway.

REFERENCE 5: 126:343813 Preparation of vitamin B12 receptor modulating agents. Morgan, A. Charles, Jr; Wilbur, D. Scott; Pathare, Pradip M. (Receptagen Corporation, USA; University of Washington; Morgan, A. Charles, Jr.; Wilbur, D. Scott; Pathare, Pradip, M.). PCT Int. Appl. WO 9714711 A1 19970424, 97 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1996-US16672 19961018. PRIORITY: US 1995-545496 19951019; US 1995-545151 19951019.

AB Vitamin B12 receptor modulating agents capable of modulating cell surface receptors by affecting the cell surface receptor trafficking pathway are disclosed. The vitamin B12 receptor modulating agents are comprised of a covalently bound rerouting moiety and targeting moiety linked by a water-solubilizing linker.

REFERENCE 6: 126:207193 Synthesis of Cobalamin Dimers Using Isophthalate Crosslinking of Corrin Ring Carboxylates and Evaluation of Their Binding to Transcobalamin. 2. Pathare, Pradip M.; Wilbur, D. Scott; Hamlin, Donald K.; Heusser, Shannon; Quadros, Edward V.; McLoughlin, Patricia; Morgan, A. Charles (Department of Radiation Oncology, University of Washington, Seattle, WA, 98195, USA). Bioconjugate Chem., 8(2), 161-172 (English) 1997. CODEN: BCCHES. ISSN: 1043-1802. Publisher: American Chemical Society.

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contg. the water-solubilizing trioxadiamine linker appeared to have avidities similar to those of the Cbl monomers.

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GI

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L5 ANSWER 6 OF 7 REGISTRY COPYRIGHT 2001 ACS
RN 173341-53-2 REGISTRY
CN Cobinamide, Ne,Ne'-[[5-[[4-(tributylstannyl)benzoyl]amino]-1,3-phenylene]bis(carbonylimino-12,1-dodecanediyl)]bis[Co-(cyano-.kappa.C)-, bis(dihydrogen phosphate) (ester), bis(inner salt), 3',3''-diester with (5,6-dimethyl-1-.alpha.-D-ribofuranosyl-1H-benzimidazole-.kappa.N3) (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:
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MF C177 H259 Co2 N31 O31 P2 Sn
CI CCS
SR CA
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
7 REFERENCES IN FILE CA (1967 TO DATE)
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Synthesis of several receptor-modulating agents using different functional classes of rerouting moieties is described. More specifically, a series of examples are presented which employ vitamin B12 as a targeting moiety in a receptor-modulating agent.

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L5 ANSWER 7 OF 7 REGISTRY COPYRIGHT 2001 ACS
RN 173341-52-1 REGISTRY
CN Cobinamide, Nb,Nb'-[[5-[[4-(tributylstannyl)benzoyl]amino]-1,3-phenylene]bis(carbonylimino-12,1-dodecanediyl)]bis[Co-(cyano-.kappa.C)-, bis(dihydrogen phosphate) (ester), bis(inner salt), 3',3''-diester with (5,6-dimethyl-1-.alpha.-D-ribofuranosyl-1H-benzimidazole-.kappa.N3) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
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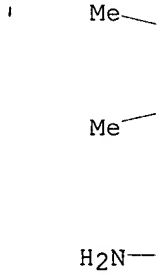

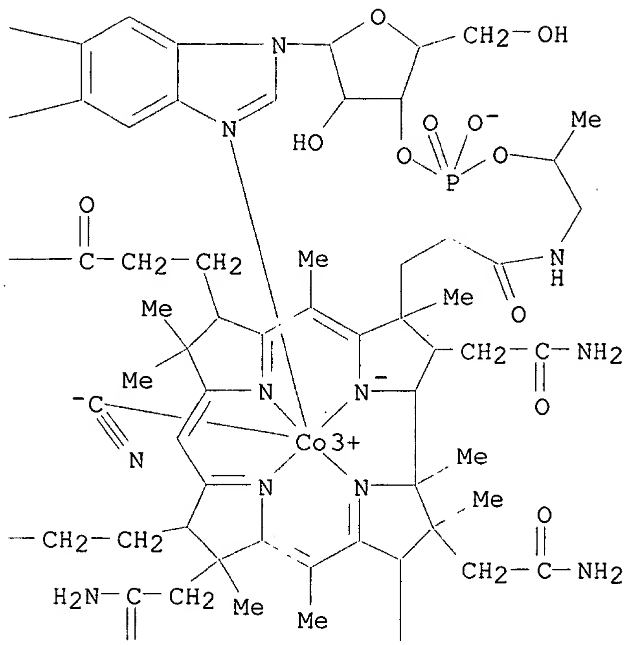
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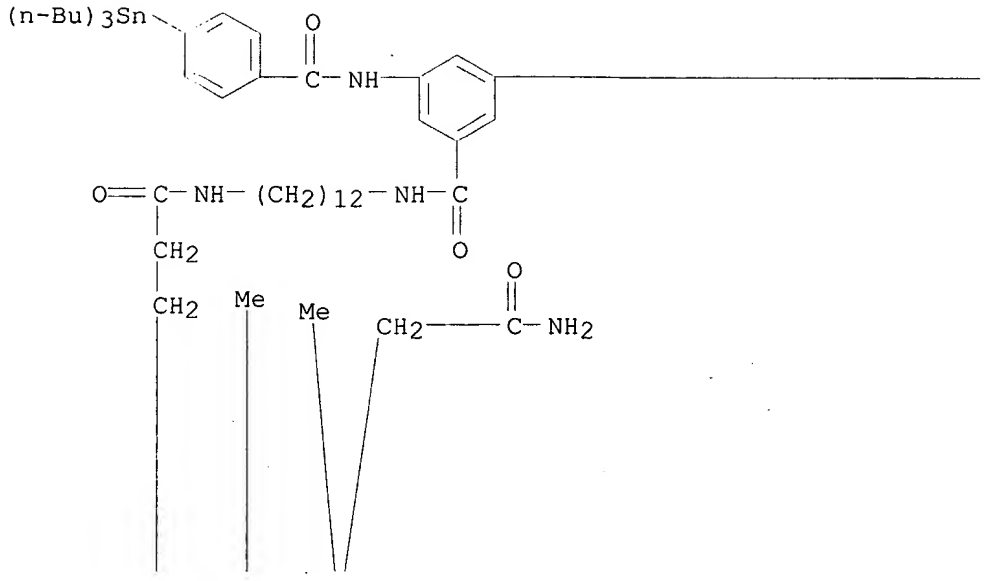

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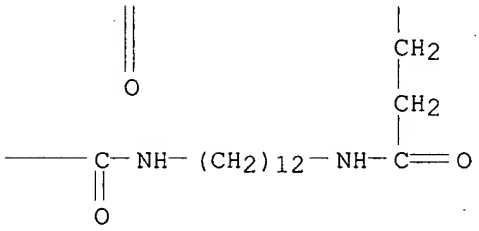

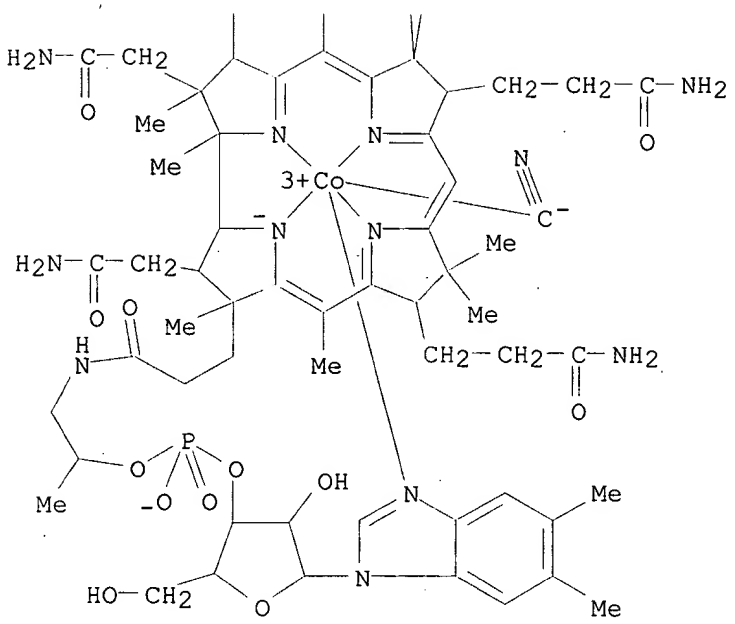

7 REFERENCES IN FILE CA (1967 TO DATE)
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AB Several cobalamin (Cbl) dimers have been prepd. for evaluation as potential antiproliferative agents in the treatment of AIDS-related lymphoma. The Cbl dimers were synthesized by crosslinking Cbl carboxylates, produced by acid hydrolysis of the b-, d-, and e-propionamide side chains of cyanocobalamin (CN-Cbl), through an isophthalate mol. Linking mols. were used between the Cbl carboxylates and the isophthalate moiety. The linkers were incorporated to provide a distance between the two Cbl mols. such that the dimeric Cbls might bind two mols. of transcobalamin II (TCII), the Cbl transport protein in plasma. Initially, the linking moiety used was 1,12-diaminododecane, but the resulting dimers had low aq. soly. To improve the soly. of the dimers, 4,7,10-trioxa-1,13-tridecanediamine was employed as the linking moiety. This improved the water soly. of the dimers considerably, while retaining the distance between the Cbl mols. at 41-42 .ANG. (fully extended). To introduce addnl. substitution on Cbl dimers, 5-aminoisophthalic acid was used as the crosslinking reagent. P-Iodobenzoyl and p-(tri-n-butylstannyl)benzoyl conjugates of 5-aminoisophthalate were synthesized and used to prep. Cbl dimers. The stannylbenzoyl-conjugated Cbl dimers were prepd. as precursors to be used in radioiodination reactions, and the iodobenzoyl-conjugated Cbl dimers were prepd. as HPLC stds. for the radioiodinated product. Attempts to iodinate/radioiodinate the stannylbenzoyl Cbl dimers were unsuccessful. Although an explanation for this is not readily apparent, the failure to react may be due to the lipophilicity of the linker used and the steric environment of the two Cbl moieties. A biotinylated deriv. of 5-aminoisophthalate was also synthesized and used to prep. biotinylated-Cbl dimers. In a competitive rhTCII binding assay with [57Co]CN-Cbl, Cbl dimers contg. the lipophilic diaminododecane linking moiety had decreased binding avidities compared to those of Cbl monomers substituted at the same corrin ring carboxylate. However, Cbl dimers contg. the water-solubilizing trioxadiamine linker appeared to have avidities similar to those of the Cbl monomers.

REFERENCE 7: 124:176815 Preparation of vitamin B12 derivatives as receptor modulating agents for treating cancers. Morgan, A. Charles; Wilbur, D. Scott; Pathare, Pradip M. (USA). PCT Int. Appl. WO 9527723 A1 19951019, 101 pp. DESIGNATED STATES: W: AU, CA, JP, KR, NO, NZ; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1995-US4404 19950407. PRIORITY: US 1994-224831 19940408; US 1995-406191 19950316; US 1995-406194 19950316; US 1995-406192
19950316.

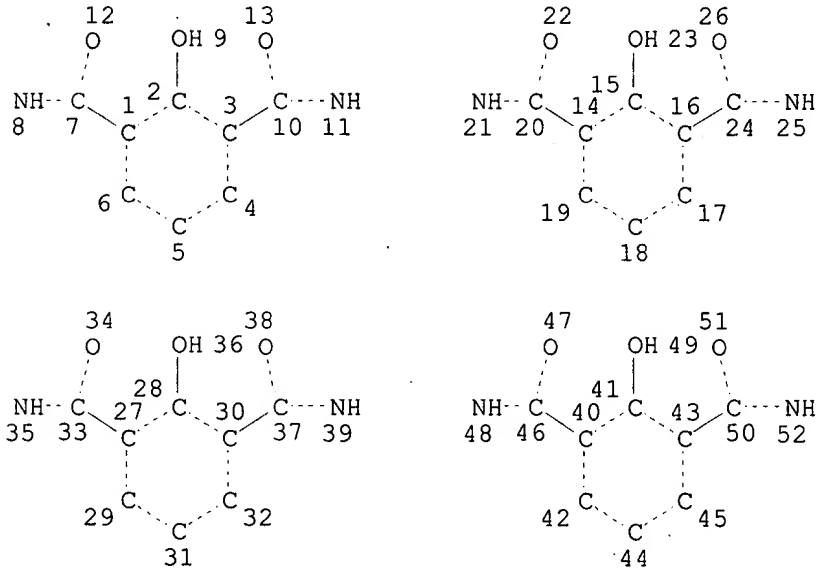
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Receptor modulating agents comprising a vitamin B12 targeting mol. coupled to a rerouting moiety (I; R1 - R7 = a linker, through which a rerouting moiety is coupled), which are capable of modulating cell surface receptors by affecting the cell surface receptor trafficking pathway via retaining an agent/receptor complex in an endosome, are prepd. Said rerouting moiety is preferably (1) a lysosomotropic moiety selected from aminoglycoside antibiotics such as gentamycin, sisomicin, netilmicin, kanamycin, tobramycin, amikacin, neomycin, paromomycin, ribostamycin, butirosin, and streptomycin, (2) a peptide sorting sequence selected from endoplasmic reticulum retention peptides, golgi retention peptides, lysosomal retention peptides, organism specific retention peptides, and clathrin-binding peptides., and (3) a conditional membrane binding peptide selected from charged glutamate, aspartate, and histidine. These receptor modulating agents are useful for treating neoplastic disorders such as leukemia, sarcoma, myeloma, carcinoma, neuroma, melanoma, cancers of the lung, liver, breast, colon, cervix, and prostate, Hodgkin's disease, and non-Hodgkin's lymphoma. Thus, a mixt. of 500 mg cyanocobalamin monocarboxylic acids I (R1 = R7 = OH, R2 - R6 = NH2; R1 = R3 - R6 = NH2, R2 = R7 = OH; R1 - R3 = R5 = R6 = NH2, R4 = R7 = OH) (prepn. given) and 3.6 g 1,12-diaminododecane in 100 mL H2O was adjusted to pH 6 with 1 N HCl, treated with 726 mg 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, and stirred at room temp. for 22 h to give cyanocobalamin monocarboxylic acid N-(12-aminododecyl)amides I [R1 = NH(CH2)12NH2, R2 - R6 = NH2, R7 = OH] and I [R1 = R3 - R6 = NH2, R2 = NH(CH2)12NH2, R7 = OH] (II). II at 10 .mu.M in vitro killed 85% K562 cells.

=> d l8 que stat;s l8 not l5

L6 STR



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NUMBER OF NODES IS 52

STEREO ATTRIBUTES: NONE
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L9 7 L8 NOT L5

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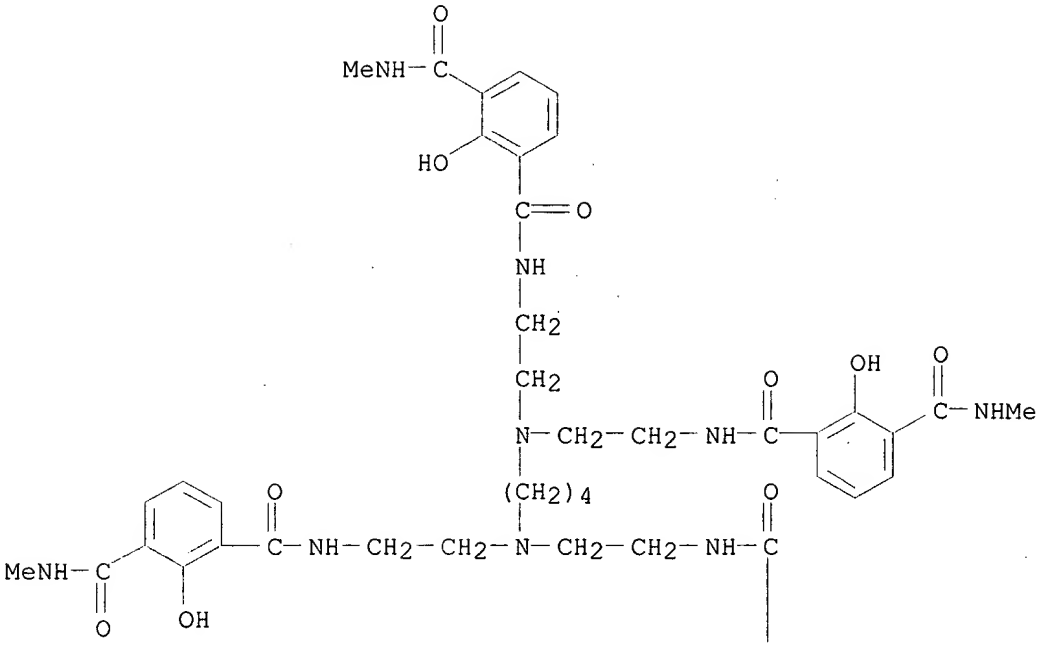
L9 ANSWER 1 OF 7 REGISTRY COPYRIGHT 2001 ACS
RN 288099-76-3 REGISTRY
CN 1,3-Benzenedicarboxamide,
N,N'',N'''',N''''''-[1,4-butanediylbis(nitrilodi-
2,1-ethanediyl)]tetrakis[2-hydroxy-N'-methyl- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C48 H60 N10 O12
SR CA
LC STN Files: CA, CAPLUS

PAGE 1-A



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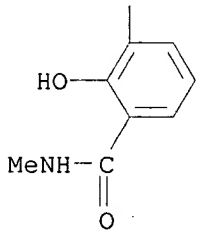

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

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MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US4258 20000218. PRIORITY: US 1999-PV120881 19990218.

GI

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AB The present invention provides luminescent lanthanide metal chelates comprising a metal ion of the lanthanide series and a macrocyclic complexing agent comprising at least one phthalamidyl moiety. Claimed are the phthalamidyl-contg. ligands, e.g., I [R1, R2, R4, R5, R6, R7, R10, R20 = H, (un)substituted alkyl with proviso for optional presence of rings; R3, R8, R9 = (un)substituted alkyl or aryl; R11, R12, R13, R21, R22, R23 = (un)substituted alkyl, H, various amines, nitro, OH, various alkoxy, etc.; Q1 = OR18 and Q2 = OR19 where R18 and R19 are H, enzymically labile group, hydrolytically labile group, neg. charge; a, z = 0 or 1 with provisos]. The compds. may incorporate recognition moieties such as polyethers and dendrimers, or are covalently attached to a carrier mol., e.g., small mol. bioactive agents, synthetic polymers and biomols., including antibodies, antigens, peptides, nucleic acids, enzymes, haptens, carbohydrates, and pharmaceutically active agents. The lanthanide metal complexes are luminescent. Also provided are probes incorporating the phthalamidyl ligands of the invention, methods using the ligands of the invention, and probes comprising the ligands of the invention. Provided are methods for detg. whether a sample contains an enzyme, whether a compd. alters an activity of an enzyme, detecting a nucleic acid target sequence, detecting amplification of a target sequence, and ascertaining whether a first nucleic acid and a second nucleic acid hybridize. Also provided are probes incorporating the phthalamidyl ligands of the invention and methods using the ligands of the invention and probes comprising the ligands of the invention. Also claimed is a microarray comprising the lanthanide complex, and said quencher being conjugated directly to a solid support or to a carrier mol. attached to the solid support, and a method for probing the microarray for the presence of a compd. Also provided are use of the complexes for radiation therapy, photodynamic therapy, as a component in an ink or dye, as a component of a substrate for transmission and amplification of light, for performing a fluorescence assay of an analyte, and for selective ion sepn. Thus, the synthesis of bicappedTRENSAM, ligand II, is presented along with the prepn. of its Eu and Tb complexes, both of which are luminescent. Other examples are provided.

L9 ANSWER 2 OF 7 REGISTRY COPYRIGHT 2001 ACS
RN 288099-75-2 REGISTRY
CN 1,3-Benzenedicarboxamide, N,N'',N'''',N''''''-[1,3-

propanediylbis(nitrilodi-2,1-ethanediyl)]tetrakis[2-hydroxy-N'-methyl- (9CI) (CA INDEX NAME)

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MF C47 H58 N10 O12
SR CA
LC STN Files: CA, CAPLUS

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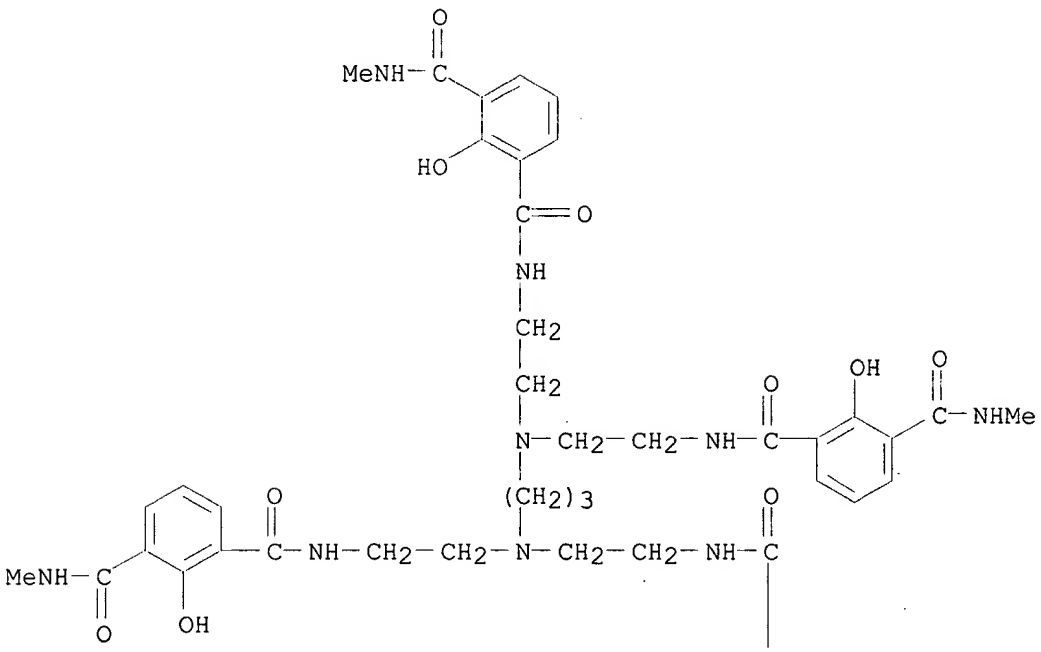

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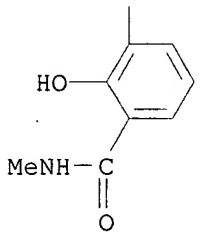

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GI

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ligand II, is presented along with the prepn. of its Eu and Tb complexes, both of which are luminescent. Other examples are provided.

L9 ANSWER 3 OF 7 REGISTRY COPYRIGHT 2001 ACS
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CN 1,3-Benzenedicarboxamide,
N,N'',N'''',N''''''-[1,2-ethanediylbis(nitrilodi-
2,1-ethanediyl)]tetrakis[N'-(6-aminohexyl)-2-hydroxy- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C66 H100 N14 O12
SR CA
LC STN Files: CA, CAPLUS

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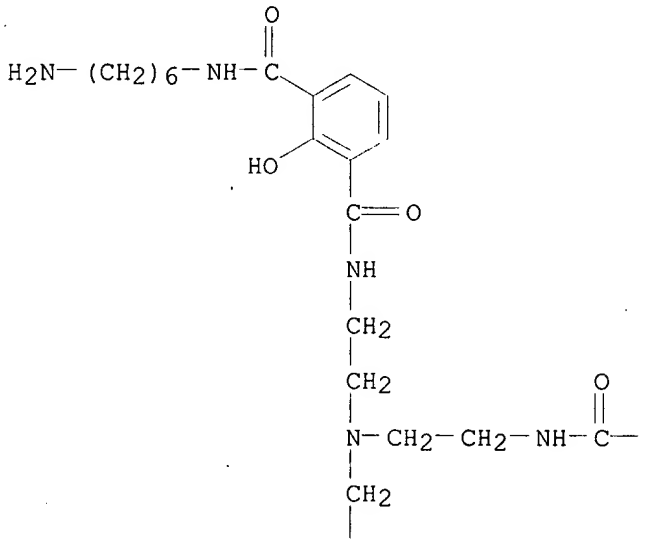

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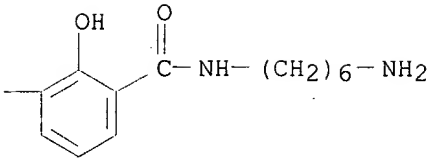

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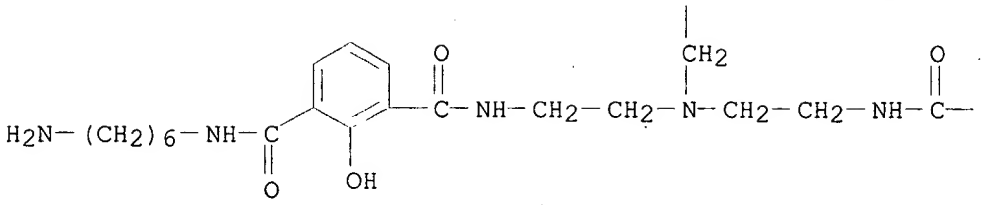

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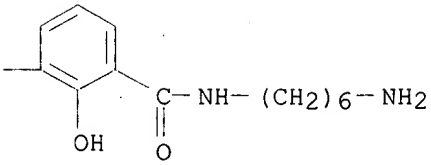

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GI

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amplification of light, for performing a fluorescence assay of an analyte,
and for selective ion sepn. Thus, the synthesis of bicappedTRENSAM, ligand II, is presented along with the prepn. of its Eu and Tb complexes, both of which are luminescent. Other examples are provided.

L9 ANSWER 4 OF 7 REGISTRY COPYRIGHT 2001 ACS
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SR CA
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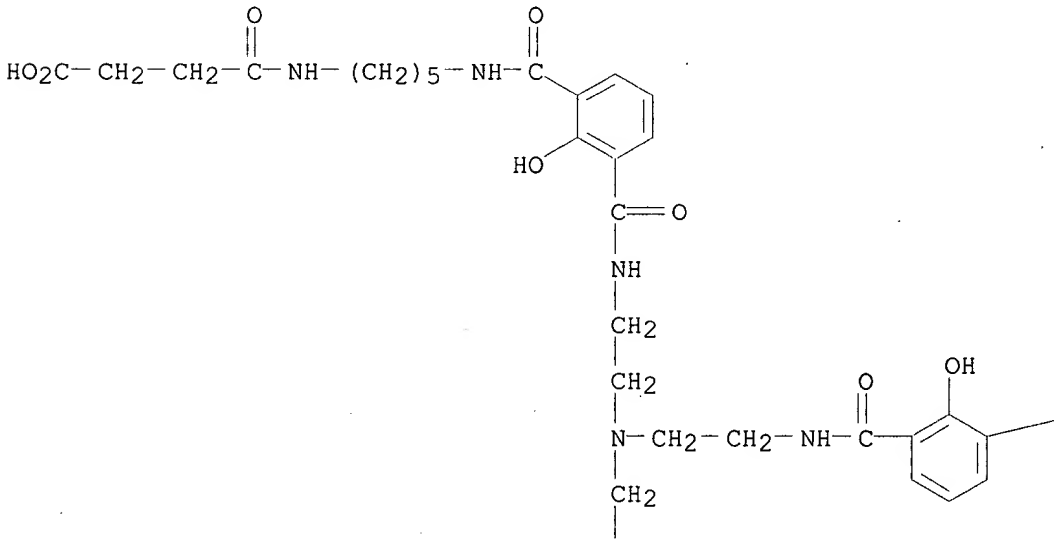

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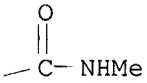

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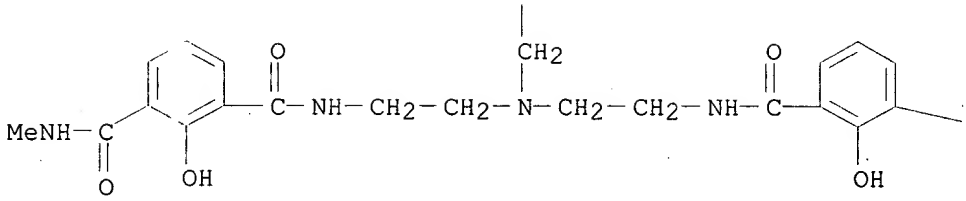

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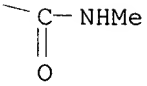

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ligand II, is presented along with the prepn. of its Eu and Tb complexes, both of which are luminescent. Other examples are provided.

L9 ANSWER 5 OF 7 REGISTRY COPYRIGHT 2001 ACS
RN 288099-68-3 REGISTRY
CN Butanoic acid, 4-[[5-[[3-[5,8-bis[2-[[2-hydroxy-3-[(methylamino)carbonyl]benzoyl]amino]ethyl]-12-[2-hydroxy-3-[(methylamino)carbonyl]phenyl]-1,12-dioxo-2,5,8,11-tetraazadodec-1-yl]-2-hydroxybenzoyl]amino]pentyl]amino]-4-oxo-, dihydrobromide (9CI) (CA INDEX NAME)
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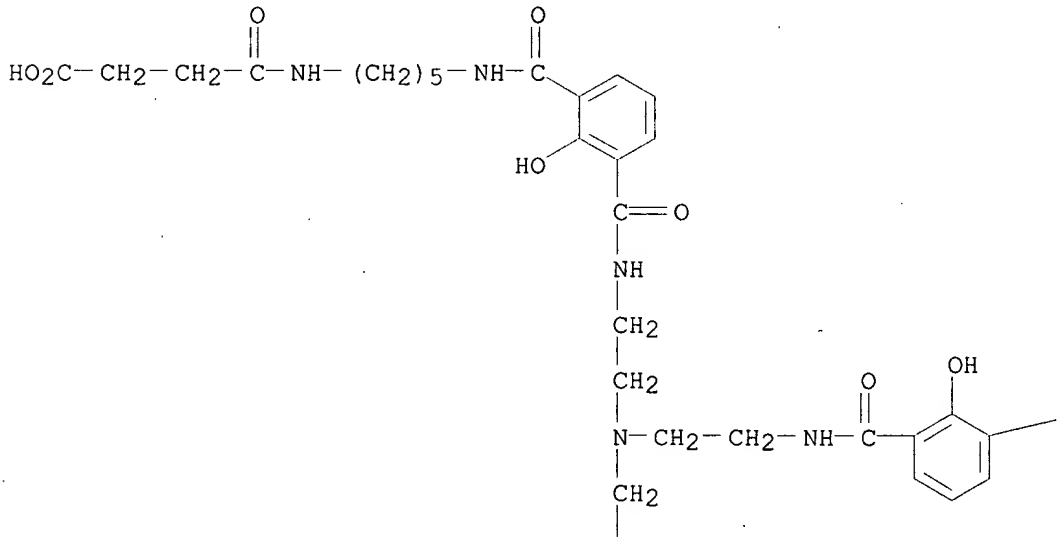
SR CA
LC STN Files: CA, CAPLUS
CRN (288099-69-4)

PAGE 1-A



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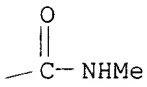

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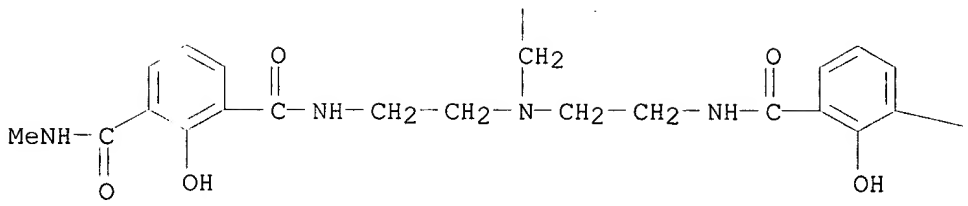
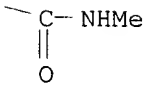


• 2 HBr

PAGE 2-B



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:171468 Phthalamide-lanthanide complexes for use as luminescent markers. Raymond, Kenneth N.; Petoud, Stephane; Cohen, Seth;

Xu, Jide (Regents of the University of California, USA). PCT Int. Appl. WO 2000048990 A1 20000824, 149 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US4258 20000218. PRIORITY: US 1999-PV120881 19990218.

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention provides luminescent lanthanide metal chelates comprising a metal ion of the lanthanide series and a macrocyclic complexing agent comprising at least one phthalamidyl moiety. Claimed are the phthalamidyl-contg. ligands, e.g., I [R1, R2, R4, R5, R6, R7, R10, R20 = H, (un)substituted alkyl with proviso for optional presence of rings; R3, R8, R9 = (un)substituted alkyl or aryl; R11, R12, R13, R21, R22, R23 = (un)substituted alkyl, H, various amines, nitro, OH, various alkoxy, etc.; Q1 = OR18 and Q2 = OR19 where R18 and R19 are H, enzymically labile group, hydrolytically labile group, neg. charge; a, z = 0 or 1 with provisos]. The compds. may incorporate recognition moieties such as polyethers and dendrimers, or are covalently attached to a carrier mol., e.g., small mol. bioactive agents, synthetic polymers and biomols., including antibodies, antigens, peptides, nucleic acids, enzymes, haptens, carbohydrates, and pharmaceutically active agents. The lanthanide metal complexes are luminescent. Also provided are probes incorporating the phthalamidyl ligands of the invention, methods using the ligands of the invention, and probes comprising the ligands of the invention. Provided are methods for detg. whether a sample contains an enzyme, whether a compd. alters an activity of an enzyme, detecting a nucleic acid target sequence, detecting amplification of a target sequence, and ascertaining whether a first nucleic acid and a second nucleic acid hybridize. Also provided are probes incorporating the phthalamidyl ligands of the invention and methods using the ligands of the invention and probes comprising the ligands of the invention. Also claimed is a microarray comprising the lanthanide complex, and said quencher being conjugated directly to a solid support or to a carrier mol. attached to the solid support, and a method for probing the microarray for the presence of a compd. Also provided are use of the complexes for radiation therapy, photodynamic therapy, as a component in an ink or dye, as a component of a substrate for transmission and

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and for selective ion sepn. Thus, the synthesis of bicappedTRENSAM, ligand II, is presented along with the prepn. of its Eu and Tb complexes, both of which are luminescent. Other examples are provided.

L9 ANSWER 6 OF 7 REGISTRY COPYRIGHT 2001 ACS
RN 288099-63-8 REGISTRY
CN 1,3-Benzenedicarboxamide, N,N'',N'''',N''''''-[1,2-ethanediylbis(nitrilodi-2,1-ethanediyl)]tetrakis[2-hydroxy-N'-methyl- (9CI) (CA INDEX NAME)
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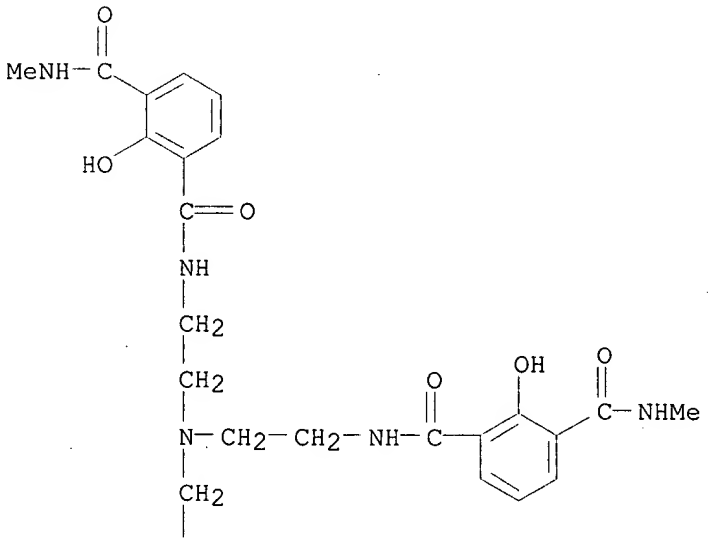
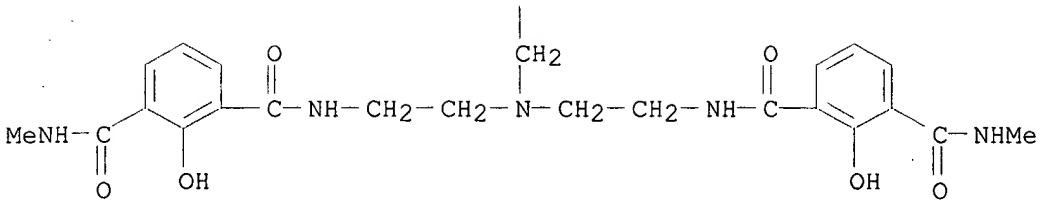
SR CA
LC STN Files: CA, CAPLUS

PAGE 1-A





1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:171468 Phthalamide-lanthanide complexes for use as luminescent markers. Raymond, Kenneth N.; Petoud, Stephane; Cohen, Seth; Xu, Jide (Regents of the University of California, USA). PCT Int. Appl. WO 2000048990 A1 20000824, 149 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US4258 20000218. PRIORITY: US 1999-PV120881 19990218.

GI

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AB The present invention provides luminescent lanthanide metal chelates comprising a metal ion of the lanthanide series and a macrocyclic complexing agent comprising at least one phthalamidyl moiety. Claimed are the phthalamidyl-contg. ligands, e.g., I [R1, R2, R4, R5, R6, R7, R10, R20 = H, (un)substituted alkyl with proviso for optional presence of rings; R3, R8, R9 = (un)substituted alkyl or aryl; R11, R12, R13, R21, R22, R23 = (un)substituted alkyl, H, various amines, nitro, OH, various alkoxy, etc.; Q1 = OR18 and Q2 = OR19 where R18 and R19 are H, enzymically labile group, hydrolytically labile group, neg. charge; a, z = 0 or 1 with provisos]. The compds. may incorporate recognition moieties such as polyethers and dendrimers, or are covalently attached to a carrier mol., e.g., small mol. bioactive agents, synthetic polymers and biomols., including antibodies, antigens, peptides, nucleic acids, enzymes, haptens, carbohydrates, and pharmaceutically active agents. The lanthanide metal complexes are luminescent. Also provided are probes incorporating the phthalamidyl

ligands of the invention, methods using the ligands of the invention, and probes comprising the ligands of the invention. Provided are methods for detg. whether a sample contains an enzyme, whether a compd. alters an activity of an enzyme, detecting a nucleic acid target sequence, detecting amplification of a target sequence, and ascertaining whether a first nucleic acid and a second nucleic acid hybridize. Also provided are probes incorporating the phthalamidyl ligands of the invention and methods using the ligands of the invention and probes comprising the ligands of the invention. Also claimed is a microarray comprising the lanthanide complex, and said quencher being conjugated directly to a solid support or to a carrier mol. attached to the solid support, and a method for probing the microarray for the presence of a compd. Also provided are use of the complexes for radiation therapy, photodynamic therapy, as a component in an ink or dye, as a component of a substrate for transmission and amplification of light, for performing a fluorescence assay of an analyte, and for selective ion sepn. Thus, the synthesis of bicappedTRENSAM, ligand II, is presented along with the prepn. of its Eu and Tb complexes, both of which are luminescent. Other examples are provided.

L9 ANSWER 7 OF 7 REGISTRY COPYRIGHT 2001 ACS
RN 288099-62-7 REGISTRY
CN 1,3-Benzenedicarboxamide, N,N'',N'''',N''''''-[1,2-ethanediylbis(nitrilodi-2,1-ethanediyl)]tetrakis[2-hydroxy-N'-methyl-, dihydrobromide (9CI) (CA INDEX NAME)
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CRN (288099-63-8)

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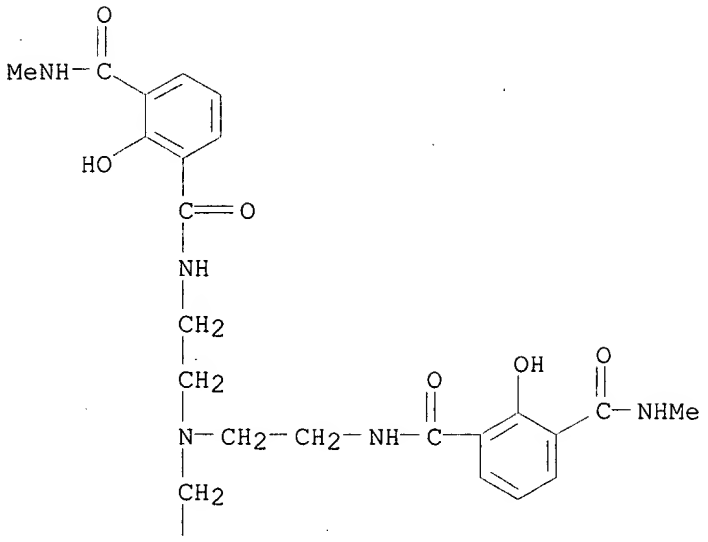

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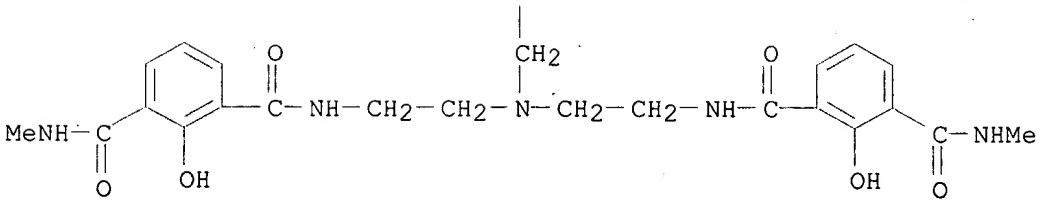

● 2 HBr

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:171468 Phthalamide-lanthanide complexes for use as luminescent markers. Raymond, Kenneth N.; Petoud, Stephane; Cohen, Seth; Xu, Jide (Regents of the University of California, USA). PCT Int. Appl. WO 2000048990 A1 20000824, 149 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT,

RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US4258 20000218. PRIORITY: US 1999-PV120881 19990218.

GI

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```
=> s ?phthalamid?/cns

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=> fil medl,caplus,biosis,embase,wpids,jicst,scisearch,inspec,compendex;s
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or lanthanide or dy or sn or tb or er or eu or nd or yb or la or gd or lu)

COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   329.89     465.15

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                    -7.84      -7.84

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FILE 'CAPLUS' ENTERED AT 14:34:08 ON 28 MAR 2001
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FILE 'COMPENDEX' ENTERED AT 14:34:08 ON 28 MAR 2001
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UM OR CHELATE OR LANTHANIDE OR DY OR SN OR TB OR ER OR EU OR ND
OR YB OR LA OR GD OR LU)
Left truncation is not valid in the specified search field in the specified file. The term has been searched without left truncation. Examples: '?TERPEN?' would be searched as 'TERPEN?' and '?FLAVONOID' would be searched as 'FLAVONOID.'

If you are searching in a field that uses implied proximity, and you used a truncation symbol after a punctuation mark, the system may interpret the truncation symbol as being at the beginning of a term. Implied proximity is used in search fields indexed as single words, for example, the Basic Index.

=> s l19 and (luminesc? or fluorescen?)

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L23 1 FILE EMBASE
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L25 0 FILE JICST-EPLUS
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L27 0 FILE INSPEC
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L30 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 1
2000:592692 Document No. 133:171468 **Phthalamide-lanthanide** complexes for use as **luminescent** markers. Raymond, Kenneth N.; Petoud, Stephane; Cohen, Seth; Xu, Jide (Regents of the University of California, USA). PCT Int. Appl. WO 2000048990 A1 20000824, 149 pp.

DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US4258 20000218. PRIORITY: US 1999-PV120881 19990218.

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L30 ANSWER 2 OF 8 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
2000359353 EMBASE Activation of retinoic acid receptor .alpha. is sufficient for full induction of retinoid responses in SK-BR-3 and T47D human breast cancer cells. Schneider S.M.; Offterdinger M.; Huber H.; Grunt T.W.. T.W. Grunt, Lab. for Cell Growth/Differentiation, Division of Oncology, Department of Internal Medicine I, Waehringer Guertel 18-20, A-1090 Vienna, Austria. thomas.grunt@akh-wien.ac.at. Cancer Research 60/19 (5479-5487) 1 Oct 2000.
Refs: 42.
ISSN: 0008-5472. CODEN: CNREA8. Pub. Country: United States. Language: English. Summary Language: English.
AB Retinoid signaling via retinoic acid (RA) and retinoid X receptors (RARs and RXRs) regulates mammary epithelial cell growth and differentiation. Loss of RAR-.beta. might represent an early event during breast carcinogenesis. Higher differentiated, estrogen-dependent, estrogen receptor (**ER**)-positive (**ER**+) mammary carcinoma cells have been found to contain relatively high levels of RAR-.alpha. and to be responsive to retinoids, whereas most undifferentiated, estrogen-independent, **ER**-negative (**ER**-) cells are characterized by low RAR-.alpha. expression and by retinoid resistance. In contrast, RAR-.gamma. is detectable at equal levels in both **ER**+ and **ER**- cells. In the present investigation, we directly examined the relative contribution of the distinct retinoid receptors to the retinoid response of breast cancer cells by comparing the effects of low concentrations of specific retinoids, which selectively activate individual receptor subtypes, on growth, cell cycle distribution, apoptosis, and on the autoregulation of RAR-.alpha. and RAR-.gamma. in **ER**- SK-BR-3 and **ER**+ T47D breast cancer cells. In vitro growth activity was determined by using a colorimetric cell viability assay and analysis of cell cycle distribution, and apoptosis was performed by flow cytometry of propidium iodide-stained or **fluorescent** Annexin V-labeled cells, respectively, whereas expression of RAR-.alpha. and RAR-.gamma. was determined by Northern blotting. Both cell lines are retinoid sensitive and express high amounts of RAR-.alpha., RAR-.gamma., and RXR-.gamma.. RAR-.alpha.-selective compounds (AM80 and AM580) inhibit cell growth, induce G1 arrest, stimulate apoptosis, and up-regulate RAR-.alpha. and RAR-.gamma. mRNA as efficiently as RAR/RXR-pan-reactive (9-cis RA) and RAR-panreactive retinoids (all-trans RA, TTNPB). Remarkably, an RAR-.alpha. antagonist (Ro 41-5253) not only blocks the RAR-.alpha.-selective agonists but also the pan-reactive compounds. In contrast, RAR-.beta.-selective (CD417), RAR-.gamma.-selective (CD437/AHPN), and RXR-.alpha.-selective (Ro 25-7386) retinoids exert no effects on the examined parameters. Thus, our results support the idea that RAR-.alpha. is the crucial receptor mediating the biological effects during retinoid signaling in both **ER**- SK-BR-3 and **ER**+ T47D human breast cancer cells.

L30 ANSWER 3 OF 8 MEDLINE
1999192545 Document Number: 99192545. Environmental risk assessment for the

widely used iodinated X-ray contrast agent iopromide (Ultravist). Steger-Hartmann T; Lange R; Schweinfurth H. (Research Laboratories, Schering AG, Berlin, Germany.) ECOTOXICOLOGY AND ENVIRONMENTAL SAFETY, (1999 Mar) 42 (3) 274-81. Journal code: EDK. ISSN: 0147-6513. Pub. country: United States. Language: English.

AB Iodinated X-ray contrast media are diagnostic pharmaceuticals that are applied to enhance the contrast between organs or vessels examined and surrounding tissues during radiography. These substances are applied in doses up to ca. 200 g per person (corresponding to approx 100 g iodine) and are rapidly excreted. In the sewage system they contribute to the burden of adsorbable organic halogens (AOX). To assess the potential environmental impact of this release, studies on environmental fate and effects were conducted for a risk assessment of the frequently used X-ray contrast medium iopromide (brand name: Ultravist). A screening test for biological degradation (OECD Screening Test 301 E) led to iopromide being classified as not readily biodegradable. Therefore, the predicted environmental concentration (PEC) in surface water was calculated in a first step. The resulting concentration of 2 microgram/liter was then compared in a second step with the predicted no-effect concentration as derived from a battery of ecotoxicity tests. In short-term toxicity tests with bacteria (Vibrio fisheri, Pseudomonas putida), algae (Scenedesmus subspicatus), crustaceans (Daphnia magna), and fish (Danio rerio, Leuciscus idus) no toxic effects were detected at the highest tested concentration of 10 g/liter. In a chronic toxicity test with D. magna no effect was observed at the highest tested concentration of 1 g/liter. Using an assessment factor of 100 the ratio between the predicted environmental concentration (PEC) and the predicted no-effect concentration (PNEC) was calculated to be </=0.0002. This low value indicates that no environmental risk has to be expected as a result of the release of iopromide into the aquatic environment. Copyright 1999 Academic Press.

L30 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2001 ACS

1999:92050 New highly luminiscent and water-soluble **lanthanide** complexes for time-resolved fluoroimmunoassays based on salicylamide-type ligands. Petoud, Stephane; Cohen, Seth M.; Raymond, Kenneth N. (Department of Chemistry, University of California, Berkeley, CA, 94720, USA). Book of Abstracts, 217th ACS National Meeting, Anaheim, Calif., March 21-25, INOR-233. American Chemical Society: Washington, D. C. (English) 1999. CODEN: 67GHA6.

AB Time-resolved fluoroimmunoassays have initiated a rapid replacement of RIA technol. in recent years (Mathis, G. Clin. Chem. 1993, 39, 1953, Hemmilla, I. J. Alloys Compnds 1995, 225, 480). The former techniques take advantage of the long lifetimes of excited-state **lanthanide** **metal** ions, which permit discrimination between the signal from the labeled samples and the **fluorescence** arising from the biol. org. components. New **lanthanide** complexes with ligands obtained by the covalent coupling between the salicylamide and 2-**hydroxyisophthalamide** moieties with polyamine backbones were synthesized. The **luminescence**, stability, and soly. of these **lanthanide** complexes will be discussed. These have numerous advantages over the complexes that are used com., including: 1) the

ligands act as both chelators and chromophores/energy transfer devices, 2)
very high quantum yields in water, 3) high stability and soly., 4) the ligands are easy to synthesize starting from inexpensive materials, and 5)
the ligand design allows for access to many derivs.

L30 ANSWER 5 OF 8 MEDLINE
97212548 Document Number: 97212548. Evaluation of single sample clearance calculations in 902 patients. A comparison of multiple and single sample techniques. Lundqvist S; Hietala S O; Groth S; Sjodin J G. (Department of Diagnostic Radiology, University Hospital, Umea, Sweden.) ACTA RADIOLOGICA, (1997 Jan) 38 (1) 68-72. Journal code: ATA. ISSN: 0284-1851.
Pub. country: Denmark. Language: English.
AB PURPOSE: To derive new formulae for the calculation of single sample clearance of the contrast medium iohexol and to compare the formulae to a selection of existing single sample clearance formulae derived for the calculation of 51Cr-EDTA and 99mTc-DTPA clearance. MATERIAL AND METHODS: Glomerular filtration rate (GFR) was calculated from total plasma clearance of iohexol used for urography in 902 patients. Two plasma samples were drawn in each patient. Automated x-ray **fluorescence** analysis equipment was used for the plasma iodine analysis. Single and multiple sample iohexol clearance values were compared. In 77 patients the
multiple sample clearance values were additionally compared to a 51Cr-EDTA
clearance performed simultaneously or within 14 days. RESULTS: The precision of the results calculated by the existing single sample clearance formulae and the derived iohexol single sample clearance formulae were essentially the same. The most precise of the derived formulae was that based on the Bak Christensen & Groth formula. The correlation between multiple sample clearance of iohexol and 51Cr-EDTA was
high (r = 0.918). CONCLUSION: Iohexol can substitute 51Cr-EDTA for GFR measurement. A valid GFR can be calculated from a single plasma sample determination of iohexol clearance using either the existing formulae or the new formulae derived from the present study.

L30 ANSWER 6 OF 8 MEDLINE
96320142 Document Number: 96320142. Capillary electrophoresis for the determination of glomerular filtration rate using nonradioactive iohexol. Rocco M V; Buckalew V M Jr; Moore L C; Shihabi Z K. (Department of Internal Medicine/Nephrology, Baptist Hospital, Bowman Gray School of Medicine of Wake Forest University, Winston-Salem, NC 27157-1053, USA.) AMERICAN JOURNAL OF KIDNEY DISEASES, (1996 Aug) 28 (2) 173-7. Journal code: 3H5. ISSN: 0272-6386. Pub. country: United States. Language: English.
AB High-performance liquid chromatography (HPLC) has been used as an alternative to the isotopic method to calculate glomerular filtration rate
(GFR). With the HPLC method, serum iohexol or iothalamate levels are measured, and the plasma clearance rate of the compound is used as a surrogate for GFR. However, HPLC is a labor-intensive procedure, which limits its usefulness in the clinical setting. Capillary electrophoresis, a newer technique in which electrophoretic separations are performed in

capillary tubes, is easier and faster than HPLC. We used capillary electrophoresis for the determination of serum iohexol levels and the calculation of GFR. Patients underwent a simultaneous 125I-iothalamate clearance test and a plasma iohexol clearance test to determine GFR. Mean GFR (+/-SD) was 70.9 +/- 29.9 mL/min (range, 14.5 to 131 mL/min) in 52 patients as determined by standard iothalamate clearance methods. For iohexol clearance, the correlation coefficient and standard error were 0.93 and 10.9 mL/min, respectively, using capillary electrophoresis compared with the iothalamate method. Capillary electrophoresis is a simple, rapid method that can be used to calculate GFR and provides results at least as accurate as those obtained by HPLC and x-ray **fluorescence**.

L30 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2001 ACS
1990:15510 Document No. 112:15510 Synthesis and characterization of solid complexes of some trivalent rare earth ions with dihydroxamic acid. Liu, Guanghua (Dep. Chem., Jiangxi Univ., Nanchang, Peop. Rep. China). Huaxue Tongbao (1), 42-3 (Chinese) 1989. CODEN: HHTPAU. ISSN: 0441-3776.
AB Ln2L3.nH2O (Ln = **La**, Ce, Pr, **Nd**, Sm, **Eu**, **Gd**, **Tb**, Tm, and Y; H2L = N,N'-dihydroxyoxalamide, N,N'-dihydroxyadipamide, and N,N'-**dihydroxyphthalamide**) were prepd. The soly. of the complexes in H2O, org. solvents, and inorg. acids, molar electrocond. IR spectra, and **fluorescence** spectra were measured.

L30 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2001 ACS
1968:448194 Document No. 69:48194 Using light transformers during optical pumping. Kotsubanov, V. D.; Naboikin, Yu. V.; Ogurtsova, L. A.; Fil, I. D. (Fiz.-Tekh. Inst. Nizkikh Temp., Kharkov, USSR). Ukr. Fiz. Zh. (Ukr. Ed.), 13(1), 58-63 (Ukrainian) 1968. CODEN: UFZHAT.
AB The use of the **fluorescent** solns. inside the laser cavity with a **Nd** rod, as converters of uv radiation to useful visible light was studied. The phosphors used were: 3-hydroxy-2-naphthoic acid, 1,5-diphenyl-3-.alpha.-naphthyl-2-pyrazoline (I); 1,5-diphenyl-3-biphenylyl-2-pyrazoline (II), 3-hydroxy-2-**naphthalamide**, 4-amino-1-naphthalene-sulfonic acid, Rhodamine 6G (III), and fluorescein (IV). The most effective were solns. of I and II (2 .times. 10-5M, EtOH). III and IV were not useful. From kinetic considerations the conclusion is reached that if probability of spontaneous emission A is not greater than 105-106/sec.-1, the concn. of mols. in an excited state is sufficient for generation threshold of **Nd** laser to be influenced by nonlinear absorption of exciting light.

=> s raymond k?/au,in;s petoud s?/au,in;s cohen s?/au,in;s xu j?/au,in

'IN' IS NOT A VALID FIELD CODE
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L35 15 FILE WPIDS
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PROCESSING COMPLETED FOR L90
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=> d cbib abs 1-4


L91  ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2001 ACS         DUPLICATE 1
2000:592693   Document No. 133:171469  Salicylamide-lanthanide complexes for
     use as luminescent markers.  Raymond, Kenneth N.; Petoud,
     Stephane; Cohen, Seth; Xu, Jide (Regents of the University of California,
     USA).  PCT Int. Appl. WO 2000048991 A1 20000824, 113 pp.  DESIGNATED
     STATES: W:  AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,
     CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN,
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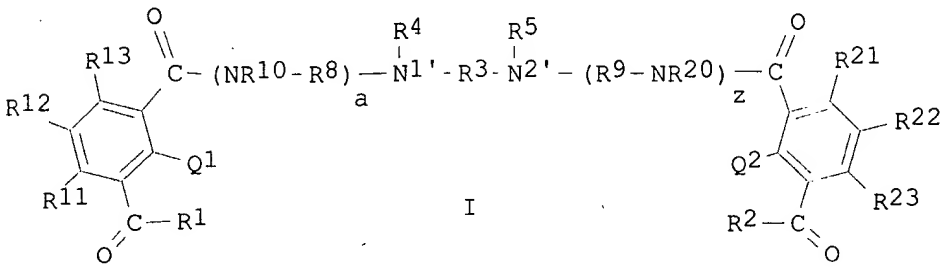
IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US4284 20000218. PRIORITY: US 1999-PV120600 19990218; US 2000-507599 20000218.

GI



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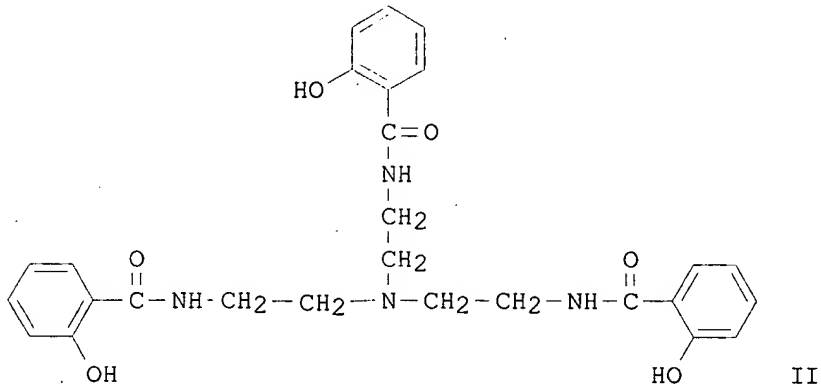

II

AB The present invention provides luminescent lanthanide metal chelates comprising a metal ion of the lanthanide series and a complexing agent comprising at least one salicylamidyl moiety. Claimed are salicylamidyl-contg. ligands, e.g., I [R1, R2 = (un)substituted alkyl, halo, hydroxy, (un)substituted alkoxy, oxy; R4, R5, R7, R10, R20 = H, (un)substituted alkyl; R3, R8, R9 = (un)substituted alkyl; R11, R12, R13, R21, R22, R23 = (un)substituted alkyl, H, various amino groups, NO2, OH, alkoxy, etc.; Q1 = OR18 and Q2 = O19 where R18 and R19 are H, enzymically labile group, hydrolytically labile group, neg. charge; a, z = 0 or 1 with various provisos]. The compds. may incorporate recognition moieties such as polyethers and dendrimers, or are covalently attached to a carrier mol., e.g., synthetic polymers and biomols., including antibodies, antigens, peptides, nucleic acids, enzymes, haptens, carbohydrates, and pharmaceutically active agents. The lanthanide metal complexes are luminescent. Also provided are probes incorporating the salicylamidyl ligands of the invention, methods using the ligands of the invention, and

probes comprising the ligands of the invention. Provided are methods for detg. whether a sample contains an enzyme, whether a compd. alters an activity of an enzyme, detecting a nucleic acid target sequence, detecting amplification of a target sequence, and ascertaining whether a first nucleic acid and a second nucleic acid hybridize. Also claimed is a microarray comprising the lanthanide complex, and said quencher being conjugated directly to a solid support or to a carrier mol. attached to the solid support, and a method for probing the microarray for the presence of a compd. Also provided are use of the complexes for radiation therapy, photodynamic therapy, as a component in an ink or dye, as a component of a substrate for transmission and amplification of light, and for performing a fluorescence assay of an analyte. The prepns. of ligand II (TRENSAM) and its Tb complex are given, as are the prepns. of several other analogs of II.

L91 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 2
2000:592692 Document No. 133:171468 Phthalamide-lanthanide complexes for use as luminescent markers. **Raymond, Kenneth N.**; Petoud, Stephane; Cohen, Seth; Xu, Jide (Regents of the University of California, USA). PCT Int. Appl. WO 2000048990 A1 20000824, 149 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US4258 20000218. PRIORITY: US 1999-PV120881 19990218.
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention provides luminescent lanthanide metal chelates comprising a metal ion of the lanthanide series and a macrocyclic complexing agent comprising at least one phthalamidyl moiety. Claimed are the phthalamidyl-contg. ligands, e.g., I [R1, R2, R4, R5, R6, R7, R10, R20 = H, (un)substituted alkyl with proviso for optional presence of rings; R3, R8, R9 = (un)substituted alkyl or aryl; R11, R12, R13, R21, R22, R23 = (un)substituted alkyl, H, various amines, nitro, OH, various alkoxy, etc.; Q1 = OR18 and Q2 = OR19 where R18 and R19 are H, enzymically labile group, hydrolytically labile group, neg. charge; a, z = 0 or 1 with provisos]. The compds. may incorporate recognition moieties such as polyethers and dendrimers, or are covalently attached to a carrier mol., e.g., small mol.

bioactive agents, synthetic polymers and biomols., including antibodies, antigens, peptides, nucleic acids, enzymes, haptens, carbohydrates, and pharmaceutically active agents. The lanthanide metal complexes are luminescent. Also provided are probes incorporating the phthalamidyl ligands of the invention, methods using the ligands of the invention, and probes comprising the ligands of the invention. Provided are methods for detg. whether a sample contains an enzyme, whether a compd. alters an activity of an enzyme, detecting a nucleic acid target sequence, detecting amplification of a target sequence, and ascertaining whether a first nucleic acid and a second nucleic acid hybridize. Also provided are probes incorporating the phthalamidyl ligands of the invention and methods using the ligands of the invention and probes comprising the ligands of the invention. Also claimed is a microarray comprising the lanthanide complex, and said quencher being conjugated directly to a solid support or to a carrier mol. attached to the solid support, and a method for probing the microarray for the presence of a compd. Also provided are use of the complexes for radiation therapy, photodynamic therapy, as a component in an ink or dye, as a component of a substrate for transmission and amplification of light, for performing a fluorescence assay of an analyte, and for selective ion sepn. Thus, the synthesis of bicappedTRENSAM, ligand II, is presented along with the prepn. of its Eu and Tb complexes, both of which are luminescent. Other examples are provided.

L91 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2001 ACS
2000:331067 Highly luminescent lanthanide complexes based on salicylamide-type ligands: Versatile molecules for luminescence applications in water.. **Petoud, Stephane; Cohen, Seth M.; Xu, Jide;** Bunzli, Jean-Claude G.; **Raymond, Kenneth N.** (Chemistry Department, U of CA, Berkeley, CA, 94720, USA). Book of Abstracts, 219th ACS National Meeting, San Francisco, CA, March 26-30, 2000, INOR-299. American Chemical Society: Washington, D. C. (English) 2000. CODEN: 69CLAC.

AB We describe here a new generation of lanthanide complexes based on salicylamide and 2-Hydroxyispothalamide ligands. Due to highly efficient energy transfer from the ligand to the lanthanide assocd. with complete protection of the cation by the ligand(s) against quenching deactivation, the luminescence properties of the lanthanide complexes can be easily exploited in water at physiol. pH. Furthermore, the stability of the complexes makes them suitable for use at very low concn. This family of ligands offers various possibilities of substitution, allowing for fine tuning of the properties of the resulting complexes. For these reasons, these compds. are very promising candidates for applications requiring highly luminescent probes possessing long lifetimes, such as homogeneous time-resolved fluoroimmunoassays or fluorescence microscopy.

L91 ANSWER 4 OF 4 SCISEARCH COPYRIGHT 2001 ISI (R)
2000:642022 The Genuine Article (R) Number: 317UV. Highly luminescent lanthanide complexes based on salicylamide-type ligands: Versatile molecules for luminescence applications in water.. **Petoud S (Reprint); Cohen S M; Xu J D;** Bunzli J C G; **Raymond K N.** UNIV CALIF BERKELEY, DEPT CHEM, BERKELEY, CA 94720;

UNIV LAUSANNE, INST INORGAN & ANALYT CHEM, CH-1015 LAUSANNE, SWITZERLAND.
ABSTRACTS OF PAPERS OF THE AMERICAN CHEMICAL SOCIETY (26 MAR 2000) Vol. 219, Part 1, pp. 299-INOR. Publisher: AMER CHEMICAL SOC. 1155 16TH ST, NW,
WASHINGTON, DC 20036. ISSN: 0065-7727. Pub. country: USA; SWITZERLAND.
Language: English.

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